Adjuvants and delivery systems in veterinary vaccinology: current state and future developments

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Table 1: Toll like receptors

Toll-like Receptor	**Structure recognised**	**TLR Location**
1	Bacterial lipoproteins	Cell surface
2	Bacterial cell wall components	Cell surface
3	Double-stranded RNA	Endosome
4	Bacterial cell wall components	Cell surface
5	Bacterial flagellin	Cell surface
6	Bacterial lipoproteins	Cell surface
7	Single-stranded RNA	Endosome
8	Single-stranded RNA	Endosome
9	Bacterial CpG DNA	Endosome

Table 2: Examples of conventional adjuvants with indication of dominant mode of action

Type	Common name or brand name	Ingredients	Mode of action*	Type of immunity (if known)
Water-in-oil emulsion				
	Freund's Complete	Mineral oil, surfactant, killed mycobacteria	D, I, Mix	Th1
	Freund's Incomplete	Mineral oil, surfactant	D	Th1
	Montanide®	Mineral oil, surfactant, immunomodulator	D, I	
	Titermax®	Squalene (metab. oil), emulsifier, block copolymer, microparticulate silica	D, I	
Oil-in-water emulsion				
	Ribi®	Squalene (metab. oil), Tween 80 surfactant, immunostim.: TDM**, MPL**, CWS**	I	
	SAF®	Squalane (metab. oil), Tween 80, block co-plymers, tMDP**	I	
	MF59	Squalene (metab. oil), Tween 80, Span 85	I	
Particles	Alum, Alhydrogel	Aluminium hydroxide Aluminium phosphate	D, I	Th2
	ISCOMs	Cholesterol, phospho-lipid, saponin Quil A, detergent and antigen 40 nm particles	D, I	Th1
	PLG microparticles	Poly[lactide-coglyco-	D	

		lide] polyester, bio-degradable Micrometer scale***		
	Alginate microparticles	Polysaccharide biodegradable Micrometer scale***	D	
	Liposomes	Phospholipid vesicles Micrometer scale***	D	
Active Compounds****				
	Saponin (Quil A, QS21)	Amphipathic, haemolytic triterpenoid saponin	M	Th1
	Monophosphoryl lipid A (MPL)	Chemically modified lipo-polysaccharide core	M, I	
	DDA	Amphiphile Dioctadecylammonium chloride	M	
	CpG	Oligonucleotide w. unmethylated CpG motif(s)	I	Th1

* Mode of action:
D: Delivery system (aggregates, particles)
I: Immunostimulatory
M: Membrane active (detergent like)
Mix: Mixed mode

**: TDM: trehalose 6,6'-dimycolate
MPL: monophosphoryl lipid A
CWS: cell wall skeleton of mycobacteria
tMDP: threonyl muramyl dipeptide

*** < 10μm: particles are efficiently taken up by APC.
>20 μm: particles ensure long-term antigen release

****often used together with other substances, e.g. microparticles

Table is based on the following references: 43, 46, 49, 120, 135, 140a